REMARKS

1 PRELIMINARY

Claims 1, 8-20, 36, 40-50, and 207-224 are pending in the application with claim 1 being independent. Claim 1 has been amended herewith. Support for the amendment may be found in the specification as Originally filed. More specifically, support may be found in Table 1, which lists all of the claimed synthetic oligonucleotides. This amendment does not introduce new matter. Applicants believe the amendment places the application in better condition for appeal.

2 REJECTIONS

A) The Rejection of Claims 1, 17, 19, and 40-44 Under 35 U.S.C. § 102(b) Should Be Withdrawn In View of Applicants' Amendment

Claims 1, 17, 19, and 40-44 stand rejected under 35 U.S.C. § 102(b) as being anticipated by *Wu et al.* (both references). The Office Action states that independent claim 1 as presently written reads on the oligonucleotide disclosed in both Wu *et al.* references. Applicants thank the Examiner for the invitation to amend the claim to clearly distinguish it over the art.

In response, Applicants have amended claim 1 to more particularly point out what Applicants believe to be the invention. Applicants' amended claim 1 now reads on a synthetic oligonucleotide selected from the group consisting of SEQ ID NOS:7-19 and 45.

Applicants believe that amended, independent claim 1 and dependent claims 17, 19, and 40-44 are not anticipated by the Wu *et al.* references; the cited reference does not disclose the specific oligonucleotides that Applicants are claiming. Applicants respectfully request reconsideration and withdrawal of the outstanding rejection under 35 U.S.C. § 102(b).

B) The Rejection of Claims 1, 13, 40-46, 48, and 50 Under 35 U.S.C. § 102(e) Should Be Withdrawn In View of Applicants' Amendment

Claims 1, 13, 40-46, 48, and 50 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Carmichael. The Office Action states on page 4, second paragraph, that claim 1 as presently written reads on the oligonucleotides that are complementary to a portion of the epsilon region of HBV genome, wherein the region of the epsilon region consists of SEQ ID NOS:7-19 and 45. The Office Action further states that claim 1 does not read on Carmichael wherein the oligonucleotides are selected from the group consisting of SEQ ID NOS:7-19 and 45.

Applicants thank the Examiner for the invitation to amend independent claim 1 to clearly distinguish it over the art. In response, Applicants have amended claim 1 to more particularly point out what Applicants believe to be the invention. Amended, independent claim 1 now reads on a synthetic oligonucleotide selected from the group consisting of SEQ ID NOS: 7-19 and 45.

Applicants believe that amended independent claim 1 and dependent claims 13, 40-46, 48, and 50 are not anticipated by the Carmichael reference; specific oligonucleotides with the sequence limitations of SEQ ID NOS:7-19 and 45 are not disclosed in this reference. Applicants respectfully request reconsideration and withdrawal of the outstanding rejection under 35 U.S.C. § 102(e).

C) The Rejection of Claims 1, 8-14, 36, 40-46, and 48-50 Under 35 U.S.C. § 103(a) Should Be Withdrawn In View of Applicants' Amendment

Claims 1, 8-14, 36, 40-46, and 48-50 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Korba *et al.*

The legal determination under 35 U.S.C. § 103 is whether the claimed invention as a whole would have been obvious to a person of ordinary skill in the art at the time the invention was made. *In re O'Farrell*, 853 F.2d 894, 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988). To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to

make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Obviousness cannot be established by hindsight combination to produce the claimed invention. *In re Gorman*, 933 F.2d 982, 986, 18 USPQ2d 1885, 1888 (Fed.Cir.1991).

Amended, independent claim 1 now reads on a synthetic oligonucleotide selected from the group consisting of SEQ ID NOS:7-19 and 45. Thus, Applicants claimed oligonucleotide has a specific sequence limitation selected from the group consisting of SEQ ID NOS:7-19 and 45. Applicants aver that the amended claim is not obvious in view of *Korba et al.* Korba *et al.* does not teach or suggest all of the physical limitations inherent to the specifically claimed oligonucleotide sequences.

In view of the amendment submitted herewith, Applicants respectfully request reconsideration and withdrawal of this outstanding rejection under 35 U.S.C. § 103(a).

D) The Rejection of Claims 1, 8-20, 36, 40-46, 48-50, 207-213, 215-222, and 224 Under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 1, 8-20, 36, 40-46, 48-50, 207-213, 215-222, and 224 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Korba *et al.* in view of Wu *et al.* (both references).

For the reasons stated *supra*, amended, independent claim 1 is non-obvious over Korba *et al.* in view of Wu *et al.* (both references). The cited references do not teach or suggest each and every element of the claimed invention. Specifically, the cited references do not teach or suggest oligonucleotides with the sequence limitations that Applicants are now claiming.

In view of the amendment submitted herewith, Applicants respectfully request reconsideration and withdrawal of this outstanding rejection under 35 U.S.C. § 103(a).

E) The Rejection of Claims 1, 45, and 47 Under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 1, 45, and 47 under stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Korba *et al.* in view of Uhlmann *et al.*

As stated *supra*, amended, independent claim 1 now reads on a synthetic oligonucleotide selected from the group consisting of SEQ ID NOS:7-19 and 45. The cited references do not teach or suggest each and every element of the claimed invention. Specifically, the cited references do not teach or suggest oligonucleotides with the sequence limitations that Applicants are now claiming.

In view of the amendment submitted herewith, Applicants respectfully request reconsideration and withdrawal of this outstanding rejection under 35 U.S.C. § 103(a).

F) The Rejection of Claims 1, 17, 19, 212, 214, 220, 221, and 223 Under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 1, 17, 19, 212, 214, 220, 221, and 223 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Korba *et al.* and Wu *et al.* (either reference) as previously applied to claims 1, 17, 19, 212, 220, and 221 and further in view of Uhlmann *et al.*

As stated *supra*, amended, independent claim 1 now reads on a synthetic oligonucleotide selected from the group consisting of SEQ ID NOS:7-19 and 45. The cited references do not teach or suggest each and every element of the claimed invention. Specifically, the cited references do not teach or suggest oligonucleotides with the sequence limitations that Applicants are now claiming.

In view of the amendment submitted herewith, Applicants respectfully request reconsideration and withdrawal of this outstanding rejection under 35 U.S.C. § 103(a).

G) The Rejection of Claims 1, 8-20, 36, 40-50, and 207-222 Under 35 U.S.C. § 102(e) Should Be Withdrawn

Claims 1, 8-20, 36, 40-50, and 207-222 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Carmichael in view of Uhlmann *et al.*

As stated *supra*, amended, independent claim 1 1 now reads on a synthetic oligonucleotide selected from the group consisting of SEQ ID NOS:7-19 and 45. The cited references do not teach or suggest each and every element of the claimed invention. Specifically, the cited references do not teach or suggest oligonucleotides with the sequence limitations that Applicants are now claiming.

In view of the amendment submitted herewith, Applicants respectfully request reconsideration and withdrawal of this outstanding rejection under 35 U.S.C. § 103(a).

H) The Rejection of Claims 8-20 and 36 under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

Claims 8-20 and 36 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants thank the Examiner for the invitation to amend independent claim 1.

In response, Applicants have amended claim 1 to more particularly point out what Applicants believe to be the invention. Applicants' amended, independent claim 1 now reads on a synthetic oligonucleotide selected from the group consisting of SEQ ID NOS:7-19 and 45.

Applicants aver that the amendment clarifying the language of claim 1 renders claims 8-20 and 36 definite. Applicants respectfully request reconsideration and withdrawal of the outstanding rejection under 35 U.S.C. § 112, second paragraph.

3 CONCLUSIONS

It is believed that all of the objections and rejections raised in the outstanding Office Action have been addressed, and the amendment and remarks provided herewith have resolved all out-standing issues in the prosecution of the captioned application. Applicants respectfully request allowance of the currently pending claims.

No additional fees are believed to be due in connection with this communication. However, please apply any additional charges, or credit any overpayment, to Deposit Account No. 50-2285. If the Examiner is of the opinion that a telephone conference

would expedite prosecution of the captioned application, the Examiner is encouraged to contact Applicants' undersigned representative.

Respectfully submitted,

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CLAIM LISTING

1. (Currently Amended) A synthetic oligonucleotide ~~complementary to a portion of the epsilon region of the HBV genome~~ selected from the group consisting of SEQ ID NOS:7-19 and 45, which oligonucleotide inhibits HBV replication.

2-7 (Canceled)

8. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:7.

9. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:8.

10. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:9.

11. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:10.

12. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:11.

13. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:12.

14. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:13.

15. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:14.

16. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:15.

17. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:16.

18. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:17.

19. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:18.

20. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:19.

21-35 (Canceled)

36. (Previously Amended) The synthetic oligonucleotide of claim 1, wherein the oligonucleotide is SEQ ID NO:45.

37-39 (Canceled)

40. (Original) The synthetic oligonucleotide of claim 1 which is modified.

41. (Original) The oligonucleotide of claim 40 wherein the modification comprises at least one internucleotide linkage selected from the group consisting of alkylphosphonate, phosphorothioate, phosphorodithioate, alkylphosphonothioate, phophoramidate, carbamate, carbonate, phosphate trimester, acetamidate, carboxymethyl ester, and combinations thereof.

42. (Original) The oligonucleotide of claim 41 comprising at least one phosphorothioate internucleotide linkage.

43. (Original) The oligonucleotide of claim 42 comprising one phosphorothioate internucleotide linkage.

44. (Original) The oligonucleotide of claim 1 which comprises at least one deoxyribonucleotide.

45. (Original) The oligonucleotide of claim 1 which comprises at least one ribonucleotide.

46. (Original) The oligonucleotide of claim 44 which comprises at least one ribonucleotide.

47. (Original) The oligonucleotide of claim 45 comprising at least one 2'-O-methyl nucleotide.

48. (Original) A kit comprising at least one oligonucleotide of claim 1.

49. (Original) A kit comprising at least two oligonucleotides of claim 1.

50. (Previously Amended) A composition comprising at least one oligonucleotide of claim 1 admixed with a pharmaceutically acceptable carrier.

51-206 (Canceled)

207. (Previously Added) The synthetic oligonucleotide of claim 16 which is modified.

208. (Previously Added) The oligonucleotide of claim 207 wherein the modification comprises at least one internucleotide linkage selected from the group consisting of alkylphosphonate, phosphorothioate, phosphorodithioate, alkylphosphonothioate, phophoramidate, carbamate, carbonate, phosphate trimester, acetamidate, carboxymethyl ester, and combinations thereof.

209. (Previously Added) The oligonucleotide of claim 208 comprising at least one phosphorothioate internucleotide linkage.

210. (Previously Added) The oligonucleotide of claim 209 comprising one phosphorothioate internucleotide linkage.

211. (Previously Added) The oligonucleotide of claim 17 which comprises at least one deoxyribonucleotide.

212. (Previously Added) The oligonucleotide of claim 17 which comprises at least one ribonucleotide.

213. (Previously Added) The oligonucleotide of claim 211 which comprises at least one ribonucleotide.

214. (Previously Added) The oligonucleotide of claim 212 comprising at least one 2'-O-methyl nucleotide.

215. (Previously Added) A kit comprising at least the oligonucleotide of claim 16.

216. (Previously Added) The synthetic oligonucleotide of claim 19 which is modified.

217. (Previously Added) The oligonucleotide of claim 216 wherein the modification comprises at lest one internucleotide linkage selected from the group consisting of alkylphosphonate, phosphorothioate, phosphorodithioate, alkylphosphonothioate, phophoramidate, carbamate, carbonate, phosphate trimester, acetamidate, carboxymethyl ester, and combinations thereof.

218. (Previously Added) The oligonucleotide of claim 217 comprising at least one phosphorothioate internucleotide linkage.

219. (Previously Added) The oligonucleotide of claim 216 comprising phosphorothioate internucleotide linkages.

220. (Previously Added) The oligonucleotide of claim 219 which comprises at least one deoxyribonucleotide.

221. (Previously Added) The oligonucleotide of claim 220 which comprises at least one ribonucleotide.

222. (Previously Added) The oligonucleotide of claim 19 which comprises at least one ribonucleotide.

223. (Previously Added) The oligonucleotide of claim 221 comprising at least one 2'-O-methyl nucleotide.

224. (Previously Added) A kit comprising at least the oligonucleotide of claim 19.

225 (Canceled)